PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 22 November 2000 (22.11.00)	
International application No. PCT/GB00/01015	**Applicant's or agent's file reference** PWC/P30184WO
International filing date (day/month/year) 17 March 2000 (17.03.00)	**Priority date** (day/month/year) 23 March 1999 (23.03.99)
Applicant CARR, Francis, J.	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

13 October 2000 (13.10.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Zakaria EL KHODARY

Telephone No.: (41-22) 338.83.38

FOR THE PURPOSES OF INFORMATION ONLY

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
PWC/P30184WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/01015	17/03/2000	23/03/1999
Applicant		
BIOVATION LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. --

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/01015

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/532 C12Q1/37 C12N15/10 C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	J M KERR ET AL: "Encoded Combinatorial Peptide Libraries Containing Non-Natural Amino Acids" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY,US,AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, vol. 115, no. 115, 24 March 1993 (1993-03-24), pages 2529-2531-2531, XP002128603 ISSN: 0002-7863 page 2530, column 1; figure 1 --- -/--	1-35

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 July 2000	08/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Hart-Davis, J

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	NIKOLAIEV V ET AL: "PEPTIDE RESEARCH. PEPTIDE-ENCODING FOR STRUCTURE DETERMINATION OF NONSEQUENCEABLE POLYMERS WITHIN LIBRARIES SYNTHESIZED AND TESTED ON SOLID-PHASE SUPPORTS" PEPTIDE RESEARCH,US,NATICK, MA, vol. 6, no. 3, 1993, pages 161-170, XP000867524 ISSN: 1040-5704 page 165; figure 1 ---	1-35
Y	WO 95 16209 A (CIBA GEIGY AG ;FELDER EDUARD (CH); RINK HANS (CH); MATTHEWS IAN TI) 15 June 1995 (1995-06-15) page 26; claim 1; example 10 page 4, line 28, paragraph 4 - line 29 ---	1-35
Y	WO 92 15679 A (PROTEIN ENG CORP) 17 September 1992 (1992-09-17) claims 1,2,26 ---	1-35
X	CAO P ET AL: "Analysis of Peptides, Proteins, Protein Digests, and Whole Human Blood by Capillary Electrophoresis/Electrospray Ionization-Mass Spectrometry Using an In-capillary Electrode Sheathless Interface" JOURNAL OF THE AMERICAN SOCIETY FOR MASS SPECTROMETRY,US,ELSEVIER SCIENCE INC, vol. 9, no. 10, 1 October 1998 (1998-10-01), pages 1081-1088, XP004140548 ISSN: 1044-0305	36,38
Y	page 1086, column 2, paragraph 2 -page 1087, column 2, paragraph 1 ---	36,37, 40-43
X	VON LEOPRECHTING ACHIM; HOERTH PATRIC; HAEHNEL WOLFGANG; SCHILZ EMILE; MUEHLENHOFF ULRICH: "Identification of biotinylation sites on proteins by selective retrieval of 2-iminobiotinylated peptides from proteolytic peptide mixtures: Localization of the accessible lysine residues on the photosystem I subunits PsaD and PsaE" ANALYTICAL BIOCHEMISTRY, vol. 262, 10 September 1998 (1998-09-10), pages 110-121, XP002143247 the whole document --- -/--	36,38, 44-51

1

C.(Continuation) DOCUMENTS CONSIDE[redacted]TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DUCRET AXEL; VAN OOSTVEEN INGE; ENG JIMMY K; YATES JOHN R III; AEBERSOLD RUEDI: "High throughout protein characterization by automated reverse-phase chromatography/electrospray tandem mass spectrometry" PROTEIN SCIENCE, vol. 7, March 1998 (1998-03), pages 706-719, XP000922504	36,38
Y	the whole document	36,37, 40-43
Y	WANG BAIYANG; CHEN YI-BEN; AYALON ORAN; BENDER JEFFREY; GAREN ALAN: "Human single-chain Fv immunoconjugates targeted to a melanoma-associated chondroitin sulfate proteoglycan mediate specific lysis of human melanoma cells by natural killer cells and complement" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 96, 16 February 1999 (1999-02-16), pages 1627-1632, XP002143248 page 1628, column 2	36,37, 40-43
P,X	GENG M ET AL: "Signature-peptide approach to detecting proteins in complex mixtures" JOURNAL OF CHROMATOGRAPHY,NL,ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, vol. 870, no. 1-2, 18 February 2000 (2000-02-18), pages 295-313, XP004187331 ISSN: 0021-9673 abstract	36,38
A	P L COURCHESNE ET AL: "Identification of Proteins by Matrix-Assisted Laser Desorption/Ionization Mass Spectroscopy Using Peptide and Fragment Ion Masses (from 2-D Proteome Analysis Protocols, Ed. A. J. Link)" METHODS IN MOLECULAR BIOLOGY,US,HUMANA PRESS INC., CLIFTON, NJ, vol. 112, no. 112, 1999, pages 487-511-511, XP002103063 page 491; figure 1	36,37, 40-43

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
P[redacted]/GB 00/01015

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9516209 A	15-06-1995	AU 1068295 A	27-06-1995
		CA 2175078 A	15-06-1995
		EP 0733213 A	25-09-1996
		FI 962371 A	07-06-1996
		HU 75223 A	28-04-1997
		JP 9508355 T	26-08-1997
		NO 962186 A	29-05-1996
WO 9215679 A	17-09-1992	US 5223409 A	29-06-1993
		JP 7501203 T	09-02-1995
		AU 1545692 A	06-10-1992
		AU 1578792 A	06-10-1992
		AU 1581692 A	06-10-1992
		AU 8740491 A	28-04-1992
		CA 2105300 A	02-09-1992
		CA 2105303 A	02-09-1992
		CA 2105304 A	02-09-1992
		DE 573603 T	06-05-1999
		EP 0575485 A	29-12-1993
		EP 0573603 A	15-12-1993
		EP 0573611 A	15-12-1993
		ES 2124203 T	01-02-1999
		JP 7501923 T	02-03-1995
		JP 6510522 T	24-11-1994
		US 5403484 A	04-04-1995
		US 5571698 A	05-11-1996
		WO 9206191 A	16-04-1992
		WO 9215677 A	17-09-1992
		WO 9215605 A	17-09-1992
		US 5663143 A	02-09-1997
		US 5837500 A	17-11-1998

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PWC/P30184WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/01015	17/03/2000	23/03/1999
International Patent Classification (IPC) or national classification and IPC G01N33/532		
Applicant BIOVATION LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 13 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
VI	☐	Certain documents cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13/10/2000	11.06.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Jacques, P Telephone No. +49 89 2399 8934

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01015

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-40 as originally filed

Claims, No.:

1-51 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-35, 37, 39-51
	No:	Claims	36, 38
Inventive step (IS)	Yes:	Claims	1-35, 37, 39-51
	No:	Claims	36, 38
Industrial applicability (IA)	Yes:	Claims	1-51
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item IV

Lack of unity of invention

1. The separate groups of invention are:
   - group 1: claims 1-15
   - group 2: claims 16-20
   - group 3: claims 21-32
   - group 4: claims 33--35
   - group 5: claims 36-51

   They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:
   - the subject-matter of claim 1 is directed to a method of protein screening of a library of individual proteins wherein the contribution over the prior art appears to be the provision of a library of individual proteins wherein each of them includes in its sequence a "barcode" allowing the identification of the said protein.
   - The subject-matter of claim 16 is also directed to a method of screening a protein library wherein the contribution over the prior art appears to be the dereplication of positively-binding pools to identify one or more individual proteins.
   - The subject-matter of claim 21 is directed to another method of protein screening wherein the contribution over the prior art appears to be the provision of a library of individual proteins wherein each of them, together with its gene, is bound to an "associating moiety".
   - The subject-matter of claim 33 is directed to a further method of protein screening wherein the contribution over the prior art appears to be the provision of a library of individual proteins wherein each of them is attached to an individual "coding moiety".

   Although the said claims are all directed to methods for screening proteins libraries, it appears that the said methods do not share any common special technical feature.

   -Moreover, the subject-matter of claim 36 is directed to a method of analysing a mixture of proteins. As the said subject-matter is already known (see point 8.1 under Item V), the subject-matter of the said claim does not provide any contribution over the prior art.

Thus, the requirements of unity of invention are not fulfilled in that there is no technical relationship among the inventions as they do not involve one or more of the same or corresponding special technical features. The expression "special technical features" means those features which define a contribution which each of the claimed inventions considered as a whole makes over the prior art.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: WO 92 15679 A (PROTEIN ENG CORP) 17 September 1992 (1992-09-17)

   D2: CAO P ET AL: 'Analysis of Peptides, Proteins, Protein Digests, and Whole Human Blood by Capillary Electrophoresis/Electrospray Ionization-Mass Spectrometry Using an In-capillary Electrode Sheathless Interface' JOURNAL OF THE AMERICAN SOCIETY FOR MASS SPECTROMETRY,US,ELSEVIER SCIENCE INC, vol. 9, no. 10, 1 October 1998 (1998-10-01), pages 1081-1088,

   D3: DUCRET AXEL; VAN OOSTVEEN INGE; ENG JIMMY K; YATES JOHN R III; AEBERSOLD RUEDI: 'High throughout protein characterization by automated reverse-phase chromatography/electrospray tandem mass spectrometry' PROTEIN SCIENCE, vol. 7, March 1998 (1998-03), pages 706-719.

2. The document cited as P-documents in the International Search Report is not to be regarded as state of the art according to Article 33(2) PCT with regard to claims 36-51, as the date of priority claimed can be allowed for these parts of the present application.
   With regard to claims 1-35, the date of priority claimed is not valid and thus the said document is part of the state of the art according to Article 33(2) PCT.

3. Document "VON LEOPRECHTING ACHIM et al., 'Identification of biotinylation sites on proteins by selective retrieval of 2-iminobiotinylated peptides from proteolytic peptide mixtures: Localization of the accessible lysine residues on the photosystem

I subunits PsaD and PsaE' ANALYTICAL BIOCHEMISTRY, vol. 262, 10 September 1998 (1998-09-10), pages 110-121" cited as an X-document in the ISR has not been considered as pertinent in the art as the said document relates to the determination of surface-exposed protein domains of proteins wherein a protein is chemically modified with 2-iminobiotin, digested by Glu-C and Arg-C protease, fractionated by avidin agarose batch and HPLC before being analysed by mass spectrometry. However, the said method is not concerned with the digestion of a protein mixture, and thus is not a method suitable for analysing mixtures of proteins.

4. Group 1 (claims 1-15) :

4.1 Notwithstanding the objection raised under Article 6 PCT (see point 2 under Item VIII), it would appear that the subject-matter of claim 15 refers to a library wherein each individual protein includes in its sequence a "barcode sequence", which can be used to identify each individual protein in the library.
As the particular combination of features of independent claim 15 is not disclosed in any cited prior art, the subject-matter of the said claim would appear to be novel (Article 33(2) PCT).

4.2 Moreover, the subject-matter of the said claim would appear to involve an inventive step in the sense of Article 33(3) PCT for the following reasons:
The closest state of the art is considered to result from document D1.
This document discloses improved libraries of display phage which display various protein domains with potential to bind to a target material of interest wherein site-specific protease cleavable linkers may be incorporated (see abstract).

The subject-matter of claim 15 is distinguished therefrom in that each individual protein includes in its sequence a "barcode sequence" and no display system is present.
The technical effect of this distinguishing feature results in identifying which protein has bound to the specific target.
The technical problem to be solved by the invention was therefore the provision of improved libraries allowing the identification of individual protein without the need of any display system.

Tha said technical problem has convincingly been solved by including in each protein of the library a "barcode sequence". As the said solution is not disclosed nor suggested in the cited prior art, the subject-matter of claim15 involves an inventive step in the sense of Article 33(3) PCT.

4.3 Notwithstanding the objection raised under Article 6 PCT (see point 1 under Item VIII), as the subject-matter of claim 1 relates to a method of screening the new and inventive protein library of claim 15 (see above points 4.1 and 4.2), the same reasoning as for the said claim applies to claim 1 which is new (Article 33(2) PCT) and involves an inventive step (Article 33(3) PCT).
The same applies to dependent claims 2-14.

5. Group 2 (claims 16-20) :

5.1 Notwithstanding the objection raised under Article 6 PCT (see point 3 under Item VIII), as the particular combination of features of independent claim 16 is not disclosed in any cited prior art, the subject-matter of the said claim would appear to be novel (Article 33(2) PCT).

5.2 Moreover, the subject-matter of the said claim would appear to involve an inventive step in the sense of Article 33(3) PCT for the following reasons:
it would appear that the technical problem to be solved is similar to the one mentioned above (see point 4.2), and has been convincingly solved by screening pools of proteins in solution, followed by the precipitation of the total pool prior to mass analysis, especially MALDI-TOF, in order to screen for a "fingerprint" of ionised peaks which is representative of the target and therefore indicates if the target has bound. A positively-binding pool is then dereplicated to reduce the complexity of the pool.

As the said solution is not disclosed nor suggested in the cited prior art, the subject-matter of claim 16 involves an inventive step in the sense of Article 33(3) PCT.

The same applies to dependent claims 17-20.

6. Group 3 (claims 21-32):

6.1 Notwithstanding the objection raised under Article 6 PCT (see point 4 under Item VIII), as the particular combination of features of independent claim 21 is not disclosed in any cited prior art, the subject-matter of the said claim would appear to be novel (Article 33(2) PCT).

6.2 Moreover, the subject-matter of the said claim involves an inventive step in the sense of Article 33(3) PCT for the following reasons:

The subject-matter of claim 21 is distinguished from the closest prior art D1 (see above point 4.2) in that a library of individual protein is screening wherein each individual protein together with its gene, is bound to an "associating moiety".
The technical effect of this distinguishing feature results in identifying which protein has bound to the target.
The technical problem to be solved by the invention is thus similar to the one mentioned above (see point 4.2).

It has convincingly been solved by binding both the protein and its gene to an "associating moiety".
As the said solution is not disclosed nor suggested in the cited prior art, the subject-matter of claim 21 involves an inventive step in the sense of Article 33(3) PCT.

The same applies to dependent claims 22-32.

7. Group 4 (claims 33-35) :

7.1 Notwithstanding the objection raised under Article 6 PCT (see point 6 under Item VIII), as the particular combination of features of independent claim 33 is not disclosed in any cited prior art, the subject-matter of the said claim would appear to be novel (Article 33(2) PCT).

7.2 Moreover, the subject-matter of the said claim involves an inventive step in the sense of Article 33(3) PCT for the following reasons:
the technical problem to be solved is similar to the one mentioned above (see point

4.2) and has been solved by the provision of a "coding moiety" wherein each individual protein of the library is attached to the said "coding moiety".

As the said solution is not disclosed nor suggestd in the cited prior art, the subject-matter of claim 33 would appear to involve an inventive step in the sense of Article 33(3) PCT.

The same applies to dependent claims 34-35.

8. Group 5 (claims 36-51) :

8.1 The subject-matter of claim 36 is not new (Article 33(2) PCT) for the following reasons:
document D2 discloses the analysis of a mixture of horse heart cytochrome c and myoglobin. The said protein mixture was first digested with trypsin, the resultant peptides were fractionated by capillary electrophoresis before being analysed by mass spectrometry (see page 1086, left column, 21 to right column, line 12).
Document D3 discloses a method for protein identification wherein enzymatic digests of either homogeneous polypeptides or simple protein mixture were generated and fractionated by reverse-phase chromatography electrospray before being analysed by mass spectrometry.
Thus, all the features of claim 36 are already known from D2 or D3.

The same applies to dependent claim 38.

8.2 The features of dependent claim 37 are not disclosed in the cited prior art, and therefore its subject-matter is considered to be new (Article 33(2) PCT).

Moreover, the subject-matter of the said claim would appear to involve an inventiv step in the sense of Article 33(3) PCT for the following reasons:
the subject-matter of the said claim differs from D2 or D3 (see above point 8.1) in that the fractionation step (ii) is carried out using a library of protein binding agents.
The technical effect of this distinguishing feature results in the fractionation of larger mixture of peptides.
The technical problem to solved was therefore to provide a method for analysing

large mixtures of peptides.

The said problem has been convincingly solved by using a library of protein binding agents to fractionate the peptides resulting from the digestion step.
As the said solution is not disclosed nor suggested in the cited prior art, the subject-matter of claim 37 would appear to involve an inventive step in the sense of Article 33(3) PCT.

The same applies to dependent claims 40, 41, 42, 43.

8.3 The features of dependent claims 39 (see however the objection under Art. 6 PCT in point 7 of Item VIII), 44, 45, 48 and 51 are not disclosed in the cited prior art, and therefore they subject-matter is considered to be new (Article 33(2) PCT).

Moreover, it would appear that all these dependent claims relate to different embodiments having the same effect as mentioned above (see point 8.2) which is the sub-fractioning of the mixture of proteins or resultant peptides.
Thus, it would appear that the technical problem to be solved by the said claims is the same as mentioned above (see point 8.2) which is to provide a method for improving the analysis of large mixtures of proteins.

As none of the cited prior art discloses nor suggests any of these embodiments for sub-fractioning a peptide mixture or peptide fragments in combination with a method for analysing mixtures of proteins, it would appear that the subject-matter of claims 39, 44, 45, 48 and 51 involve an inventive step in the sense of Article 33(3) PCT.

The same applies to dependent claims 46, 47, 49 and 50.

Re Item VII

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D3 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

1. The subject-matter of claim 1 is not clear (Article 6 PCT) for the following reasons:
- the subject-matter for which the protection is sought is not defined. A method claim should be defined in the procedural steps necessary to carry out the said method,
- furthermore, the term "barcode sequence" is vague and unclear for the skilled man and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear.

2. The subject-matter of claim 15 is not clear (Article 6 PCT) for the following reasons:
- the subject-matter of the said claim is directed to a library of proteins. The said library is defined by referring to claims directed to steps of a method for screening the said library.
Thus, as the said claim does not clearly define the library by mentioning all its essential technical features, the definition of the subject-matter of said claim is unclear.

3. The subject-matter of claim 16 is not clear (Article 6 PCT) for the following reasons:
- the subject-matter for which the protection is sought is not defined. A method claim should be defined in the essential procedural steps necessary to carry out the said method, in the present case, for example, that pool of proteins are precipitated, and then analysed by mass spectrometry to screen for a fingerprint of ionised peaks which is representative of the target, positively-binding pools being dereplicated to reduce the complexity of the pool.
- furthermore, the term "dereplication" is vague and unclear for the skilled man and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear.

4. The subject-matter of claim 21 is not clear (Article 6 PCT) for the following reasons:
- the subject-matter for which the protection is sought is not defined. A method claim should be defined in the procedural steps necessary to carry out the said method,
- furthermore, the term "associating moiety" is vague and unclear for the skilled man and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear.

5. The subject-matter of claim 23 is unclear (Article 6 PCT) as the term "dereplicated" is vague and unclear for the skilled man and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear.

6. The subject-matter of claim 33 is not clear (Article 6 PCT) for the following reasons:
- the subject-matter for which the protection is sought is not defined. A method claim should be defined in the procedural steps necessary to carry out the said method,
- furthermore, the term "coding moity" is vague and unclear for the skilled man and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear.

7. The subject-matter of claim 39 is not clear (Article 6 PCT) for the following reasons:
- the said claim is directed to the addition of one or more amino acids to the resultant peptides. However, as all the essential steps of this method are not defined (notably the step of terminal protease cleavage, as described on page 23 of the description), the subject-matter for which the protection is sought is not clearly identified. A method claim should be defined in the essential procedural steps necessary to carry out the said method.